AMENDMENTS TO THE SPECIFICATION

Please replace line 15 of page 4 with the following amended paragraph:

Fig. 5c is a graph showing the amino acid composition of the ~~G-CSF~~ **hG-CSF**;

Please replace the second full paragraph on page 6 with the following amended paragraph:

The protein level changes before and after overproducing the human-derived leptin of *E. coli* BL21(DE3)(pEDOb5) was compared by two-dimensional electrophoresis according to a known method (Hochstrasser et al., Anal. Biochem., 173:424-35, 1988; Han et al., J. Bacteriol., 183:301-8, 2001): That is, after pre-culturing of the *E. coli* BL21(DE3)(pEDOb5), expression of leptin was induced and cultured at a high concentration. A culture broth is taken before and after the induction of expression. Each culture broth is centrifuged at 6000 rpm for 5 minutes at 4°C to obtain precipitations, which were washed with 500 μl of low salt buffer (KCl 3mM, KH_2PO_4 1.5mM, NaCl 68mM, NaH_2PO_4 9mM). Then, the product was suspended in 200 μl of TE buffer (Tris-HCl 10mM, EDTA 1mM). The suspension is sonicated with a sonicator and centrifuged at 12,000 rpm for 10 minutes at 4 °C. The supernatant was discarded and ~~the solid was dried *in vacuo* and~~ **cell pellets were** stored at -20 °C, which ~~was~~ **were** used as a sample for the subsequent test.

Please replace the first full paragraph on page 7 with the following amended paragraph:

The two-dimensional gel was stained with a silver staining kit (Amersham Biosciences, Uppsala, Sweden), scanned with a scanner (GS710 Calibrated Imaging Densitometer, Bio-Rad

Laboratories Inc., USA) and subjected to a quantitative analysis of protein by Melanie II software (Bio-Rad Laboratories Inc., USA). Also, for protein identification, desired proteins were taken selectively from the two-dimensional gel, washed, dried ~~*in vacuo*~~ **in a vacuum** and reacted with trypsin for 8 hours or more at 37 °C. Then, peptides cut by trypsin were measured for their molecular weights using MALDI-TOF MS(Matrix Assisted Laser Desorption/Ionization Time of Flight mass spectrometer) (Voyager™ Biospectrometry, Perseptive Biosystems Inc., USA). The protein levels before leptin expression were compared with those of the maximum content of leptin.

Please replace the paragraph bridging page 7 and page 8 with the following amended paragraph:

As a result, it was shown that synthesis of substantially ~~all~~ **most** of the amino acids was inhibited after leptin gene expression. Particularly, the levels of enzymes involved in the synthesis of serine family amino acids (CysK, GlyA) were considerably reduced by excessive production of leptin protein, in which GlyA was reduced by 2.5 times and CysK was reduced by 2.3 times (Fig. 1). From these, it was noted that the biosynthesis of serine family amino acids was considerably impeded by the excessive production of leptin and thus, in order to promote metabolism related to reduced biosynthesis of serine family amino acids in the strain producing leptin, the serine-rich protein, the *cysK* gene encoding the CysK protein which is a critical enzyme in this pathway was to be introduced.

Please replace the first full paragraph on page 8 with the following amended paragraph:

The recombinant plasmid pAC104CysK to express the CysK protein was prepared as follows: Firstly, polymerase chain reaction (PCR) was conducted using the *E. coli* BL21(DE3) **(Novagen, Inc. (Madison, WI)** chromosome as a template, and primer 1: 5' - gcgaattcatgagtaagatttttgaagataa-3'(SEQ ID NO: 1) and primer 2: 5' - gcgaattctatatactgttgcaattctttctc-3'(SEQ ID NO: 2). Here, the first denaturation was conducted once at 95 °C for 5 minutes and the second denaturation was conducted by repeating 30 cycles of holding at 95 °C for 50 seconds, annealing at 55 °C for 1 minute and extension at 72 °C for 1 minute and 30 seconds, and then the final extension was once conducted at 72 °C for 5 minutes. The *cysK* gene thus obtained was cut with the restriction enzyme *Eco*RI and the resulting segment was inserted into the plasmid p10499A (Park et al., FEMS Microbiol. Lett., 214:217-22, 2002) having the *gntT104* promoter (Peekhaus and Conway, J. Bacteriol., 180:1777-85, 1998), which had been digested with the same restriction enzyme, to form the plasmid p104CysK. Then, the plasmid was cut with the restriction enzymes *Eco*RV and *Sca*I and cloned into the plasmid pACYC184 **(Clontech Labortories, Mountain View, CA)** digested with the restriction enzyme *Eco*RV. The product was transformed into *E. coli* XL1-blue **(Stratagene Cloning Systems, La Jolla, CA)** to prepare recombinant plasmid pAC104CysK(Fig. 2).

Please replace the first full paragraph on page 9 with the following amended paragraph:

In order to express IL-12p40(interleukin 12 β chain) protein, the recombinant plasmid pEDIL-12p40 was prepared as follows. PCR was conducted using plasmid pUC18/p40

(Cytokine bank) (http://cytokine.chonbuk.ac.kr/main3.htm) including human interleukin β chain gene as a template, and primer 3: 5'-ggctagcattaatgatatgggaactgaagaaagat-3'(SEQ ID NO: 3) and primer 4: 5'-gccggatccttattaactgcagggcacaga-3' (SEQ ID NO: 4) by following the same procedures as in Example 2 to obtain the IL-12p40 gene. The gene was digested with restriction enzymes *Ade*I and *Bam*HI. The resulting segment was inserted into the leptin expression vector **pEDOb5** (Jeong and Lee, Appl. Environ. Microbiol., 65:3027-32, 1999), which had been digested with restriction enzymes *Nde*I and *Bam*HI, to form plasmid pEDIL-12p40 (Fig. 3).

Please replace the first full paragraph on page 10 with the following amended paragraph:

Each of the transformed *E. coli* strains was inoculated into a 10 mL of R/2 medium (KH_2PO_4 6.75g/L, $(NH_4)_2HPO_4$ 2g/L, citric acid 0.85g/L, trace metal solution (HCl 5M, $FeSO_4 \cdot 7H_2O$ 10g/L, $CaCl_2$ 2g/L, $ZnSO_4 \cdot 7H_2O$ 2.2g/L, $MnSO_4 \cdot 5H_2O$ 0.54g/L, $CuSO_4 \cdot 5H_2O$ 1g/L, $(NH_4)Mo_7O_{24} \cdot 4H_2O$ 0.1g/L, $Na_2B_4O_7 \cdot 10H_2O$ 0.02g/L), 5mL/L, $MgSO_4 \cdot 7H_2O$ 0.7g/L) with 10g/L of glucose, cultured at 37 °C for overnight, transported to 200mL of R/2 medium with 10g/L of glucose and cultured at 37 °C for 8 hours. Then, 200 mL of the recombinant *E. coli* which had been cultured in the R/2 medium was inoculated into 1.8L of R/2 medium with 10g/L of glucose and cultured in an incubator kept at 37 °C and pH 6.88 while supplying a stock solution containing 700g/L of glucose and 20g/L of $MgSO_4 \cdot 7H_2O$. Here, the stock solution was supplied according to changes of pH. For instance, when pH of the medium was 6.88 or more, the stock solution was automatically adjusted and supplied at rate of 10 mL/min so that the glucose concentration in the fermentation chamber would be 0.7g/L. Air and pure oxygen were automatically adjusted and supplied to maintain the dissolved oxygen (DO) in the medium at 40%. When the optical density (O.D.) of the culture broth as measured at 600 nm using a spectrophotometer was 30, 1mM of IPTG(isopropyl-β-thiogalactoside) was added thereto to

induce expression of leptin protein. In all the cultures, 100 mg/L of ampicillin and 30 mg/L of chloramphenicol **were added** to stabilize plasmids.

Please replace the paragraph bridging page 11 and page 12 with the following amended paragraph:

According to reports, leucine and alanine are prevalent in the average composition of amino acids of *E. coli* proteins (leucine 10.5% and alanine 9.6%) and serine is 5.6% on the average (Fig. 5a, Fig. 5b, Fig. 5c and Fig. 5d). Figs. 5a to 5d are graphs showing compositional ratio of amino acids of proteins known up to date, in which Fig. 5a shows compositional ratio of amino acids of *E. coli* proteins, Fig. 5b shows compositional ratio of amino acids of leptin, Fig. 5c shows compositional ratio of amino acids of ~~G-CSF~~ **hG-CSF** and Fig. 5d shows compositional ratio of amino acids of IL-12p40.

Please replace the first full paragraph on page 12 with the following amended paragraph:

As shown in Fig. 5b, the leptin protein, which is one of typical serine-rich proteins, comprises exceptionally ~~much~~ **high** serine amino acid, in which the compositional ratio of serine is 11.6%. As shown in Fig. 5c, another known protein hG-CSF (human granulocyte-colony stimulating factor) comprises mainly 19% of leucine and 12% of alanine which are similar to proteins in *E. coli*, though it contains 8.2% of serine. As shown in Fig. 5d, another protein IL-12p40 which is also known as a serine-rich protein contains 11.1% of serine.

Please replace the paragraph bridging page 12 and page 13 with the following amended paragraph:

Fig. 6a is a graph showing changes in cell density, dry cell weight and foreign protein quantity according to the culture time, when the IL-12p40-producing recombinant *E. coli*, BL21(DE3)(pEDIL-12p40), is cultured and Fig. 6b is a graph showing changes in cell density, dry cell weight and foreign protein quantity according to the culture time, when the recombinant *E. coli* BL21(DE3)(pEDIL-12p40)(pAC104CysK) that can produce IL-12p40 and coexpress the *cysK* gene, is cultured, in which (■) represents the optical density of cells, (○) represents the dry cell weight and (▲) represents the amount of prepared interleukin 12 β chain. As shown in Fig. 6a, when IL-12p40 was produced according to the method of Example 4 except for using pEDIL-12p40 prepared in Example 3, the expression of IL-12p40 reached the peak after 7 hours from induction. From this, it was found that the production yield was 0.090 g/L•h. On the other hand, as shown in Fig. 6b, when IL-12p40 was produced according to Example 4 except for using pAC104CysK prepared in Example 2 and pEDIL-12p40 prepared in Example 3, the expression ~~reaches~~ **of IL-12p40** reached the peak after 2 hours from induction, at the maximum yield of 0.349 g/L•h.

Please replace the second full paragraph on page 13 with the following amended paragraph:

As described above, a particular part of the present invention is explained in detail. However, it is apparent to those skilled in the art that such concrete description is only for preferred embodiments and the present invention is not limited thereto. For example, as a method for overexpressing cysteine synthase, introduction of the *cysK* gene into a foreign protein expression vector or fusion **of *cysK* gene with** ~~into~~ a chromosome of a host cell may achieve the same effect if the expression amount of the *cysK* gene **is sufficient**. Therefore, the actual scope of the present invention is defined by the attached claims and equivalents thereof.